UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/692,084	08/08/96	RODRIGUEZ M	1199-1-001-C

EXAMINER	
DUFFY, P	
ART UNIT	PAPER NUMBER
1645	19

HM12/0402

DAVID A JACKSON
KLAUBER AND JACKSON
411 HACKENSACK AVENUE
HACKENSACK NJ 07601

DATE MAILED: 04/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/692,084			

EXAMINER	
ART UNIT	PAPER NUMBER
	19

DATE MAILED:

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☐ THE PERIOD FOR RESPONSE:

a) ☐ is extended to run _____ or continues to run _____ from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☒ Applicant's response to the final rejection, filed _____ has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☒ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because:

   a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

   b. ☒ They raise new issues that would require further consideration and/or search. (See Note).

   c. ☐ They raise the issue of new matter. (See Note).

   d. ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: _____

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☒ Upon the filing an appeal, the proposed amendment ☐ will be entered ☒ will not be entered and the status of the claims will be as follows:
   Claims 5-8, 15-18 withdrawn from consideration
   Claims allowed: _____
   Claims objected to: _____
   Claims rejected: 1-4, 9-14 - 19

   However;

   ☒ Applicant's response has overcome the following rejection(s): see attached

4. ☒ The ~~affidavit, exhibit or~~ request for reconsideration has been considered but does not overcome the rejection because see attached.

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

Response to Advisory Action:

1. The proposed amendment raises new issues under 112, first paragraph in view of the proposed insertion of "isolated", see elaboration below.

2. The rejection of claims under 112, second paragraph would overcome the rejection of record over "characteristic".

3. The rejection of claims 5-8 under 112, first paragraph as not enabled is maintained for reasons made of record.

Applicants arguments have been carefully considered but are not fully persuasive. Applicants have not yet established the unrestricted public availability of 01 and 04. Applicants indicate that evidence should be forthcoming. This part of the rejection is maintained until such time as persuasive evidence is provided. Applicants argue that the prior patent '629 teaches how to screen and that the courts have stated that screening is routine experimentation. As to isolated or synthetic autoantibodies, the specification fails to teach how to make isolated or synthetic autoantibodies with the characteristics of the monoclonal antibodies of the claims. The specification fails to teach from which animal these autoantibodies can be isolated. Autoantibodies are generally polyclonal and not monoclonal in nature. The population of autoantibodies from one outbred animal to another differs because the antibody genetic repertoire differs. Thus, the specification fails to teach how to predictably and reproducibly make a polyclonal antibody with the characteristics of the monoclonal antibody. Moreover, the art teaches that making polyclonal antibodies is unpredictable. The art specifically teaches that the production of polyclonal antiserum is variable and not readily reproducible. Autoantibodies are innately a polyclonal antibody population, and as such proposed amendment to recite isolated raises a new enablement issue. Isolated autoantibodies are essentially polyclonal in nature, and the art teaches that the production of that is not predictable or reproducible. The specification lacks demonstration of methods to predictably and reproducibly make polyclonal antiserum or isolated autoantibodies which have the properties of "capable of stimulating the proliferation of glial cells in the central nervous system" as is now claimed.

Applicants argue that the specification teaches how to make isolated or synthetic autoantibodies and points to pages 7-11 by using conventional methods. Conventional methods utilize antigen immunization and no antigen is described in any sufficient manner in order to be able to make isolated autoantibodies or synthetic autoantibodies by any conventional methodology in the art. This is also not persuasive because the passage cited by applicant does not define isolated autoantibody or synthetic autoantibody as an engineered or manipulated antibody as alleged. The term is given its broadest reasonable interpretation of the art. The broadest interpretation of autoantibody is an isolated polyclonal antibody or synthetic polyclonal antibody, neither of which is enabled for reasons already made of record. Given the evidence provided by the examiner and that the specification does not teach provide any evidence that the instantly claimed antibodies can predictably and reproducibly made as asserted using conventional technology which have the property of capable of inducing remyelination of central nervous system axons. Applicants argue that the generation of polyclonal antibodies are the first step in the generation of monoclonal antibodies, while this may be true for classical production of monoclonal antibodies using antigen injection it is not true in view of the teachings of the specification. The monoclonal antibodies of the specification were not sensitized to any antigen, but were apparently developed from immortalized splenocytes in the absence of any antigen immunization. Thus, the production of monoclonal antibodies is not precede by polyclonal antibody generation according to methods of making monoclonal antibodies of the specification. The specification teaches how to screen for monoclonal antibodies and does not teach how to make or screen for

isolated polyclonal autoantibodies or synthetic polyclonal antibodies with the instantly claimed properties. Applicants allege that the specification teaches animal models which are susceptible to demyelinating disease and others are demyelination refractive, it would be readily clear to one of skill in the art as to which animals to use to generate such autoantibodies. This is not persuasive, the courts have held that:

> "However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It meas that the omission of minor detains does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material *or of any conditions under which a process can be carried out,* [emphasis added] undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research." (Genentech Inc. v. Novo Nordisk A/S Ltd., 42 USPQ2d 1001).

In the instant case there is no disclosure of antigen for which isolated or synthetic polyclonal autoantibodies may generated nor any specific animals which generate autoantibodies with the remyelinating properties, undue experimentation is required.

The specification remains not enabled for isolated polyclonal (autoantibodies) or synthetic autoantibodies which are capable of inducing glial cell proliferation in central nervous system axons and the rejection is maintained.

4. The rejection of the claims under 35 U.S.C. 102(b) as being anticipated by a variety of references is maintained for reasons already made of record.

Applicants state that the instant claims are indeed entitled to the priority date of the parent application and provide citations of passages from the parent which has issues as US Patent No., 5,591,629.

Applicants point to column 2, for written description for SCH 94.03, column 8, for O4 and A2B5 and column 9 for isolated or synthetic autoantibodies. This is not persuasive because there is no conception of the use of antibodies 04 or A2B5 in the treatment method, nor any indication in these passages that these antibodies have the property of stimulating glial cell proliferation. Using the antibodies to detect cell markers provides no written descption support for their conception for use by the instantly claimed methods. Citation of use of the antibodies to characterize and antigen does not provide written description support for the use of the antibody as a pharmaceutical agent in the methods as instantly claimed. The passages cited by applicants do not provide for the use of the antibodies in the instantly claimed methods, nor does it logically flow from these passages of specification. Applicants' attempt to rely antibodies discussed in prior art references but have no written description in the priority document specification as originally filed as argued for 01 and HNK-1 is not persuasive. It is the parent specification that must provide written description, not references cited therein. These alleged references have not been properly incorporated by reference, nor does the specification of the parent document point to these specific antibodies for use as therapeutic agents for stimulating glial cell proliferation. As to passage for isolated or synthetic autoantibodies, the passage again not conceptualize the use of isolated or synthetic antibodies in a method of treatment and provides no written description for synthetic autoantibodies and merely discusses the background of the art and not specific isolated or synthetic autoantibodies.

Priority to the parent documents for the instantly claimed subject matter. The rejections are maintained.

5. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Patricia A. Duffy, Ph.D.
March 31, 1999

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600